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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/521,524	03/08/2000	Beverly L. Davidson	875.025US1	1091

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EXAMINER	
FOLEY, SHANON A	

ART UNIT	PAPER NUMBER
1648	28

DATE MAILED: 03/11/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/521,524	Applicant(s) DAVIDSON ET AL.	
	Examiner Shanon Foley	Art Unit 1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 January 2002 and 27 December 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *36-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *36-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *18,19* .
4) ☒ Interview Summary (PTO-413) Paper No(s). 28 .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The request filed on 11/25/02 for a Request for Continued Examination (RCE) under 37 CFR 1.114 based on parent Application No. 09/521524 is acceptable and a RCE has been established. An action on the RCE follows.

It is requested that when applicant submit amended or new claims to the Office, applicant list the clean version of the claims first and the marked-up version of the claims as an appendix to the amendment. This aids in eliminating confusion for determining which changes have been made. Applicant's compliance with this request is very much appreciated.

Claim Objections

The numbering of claims is not in accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. When claims are canceled, the remaining claims must not be renumbered. When new claims are presented, they must be numbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not).

Misnumbered claims 26-34 presented with the filing of the RCE on 11/25/02 have been renumbered 27-35. These claims have been cancelled in a paper submitted by applicant on March 3, 2003.

In the response filed 12/18/02, applicant submitted new claims 27-34, which have been renumbered 36-43 and are under consideration.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 36-38 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claim 36 requires that the shuttle plasmid is present in an amount fifteen times greater than the backbone plasmid. Applicant states that support for this claim is found on page 5, line 7. However, after a careful review of the disclosure at the cited passage, it cannot be determined where this limitation can be found. The passage states that the shuttle and backbone plasmids are present in amounts of 15 and 4 μg, respectively. Although this would imply that the shuttle plasmid is present in amounts four times greater than the backbone plasmid, there is no indication that the shuttle is present in amounts fifteen times greater than the backbone plasmid. There is no other mention of plasmid rations within the specification. Therefore, this claim limitation constitutes new matter. This rejection also affects dependent claims 37 and 38.

Claims 38-43 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims list a number of adenovirus backbone plasmids. The specific plasmids listed are not known in the art. It is also not evident from the teachings in the specification that the skilled artisan would be able to make the plasmids claimed. Page 8, line 18 to page 9, line 26, describe the components of each plasmid vector, but do not teach how the plasmids are generated. For example, pacAd5 9.2-100/Swa1, discussed on page 8, lines 22-24, comprises a "Pac1-Not1 site SV40pA signal Sal1-SacII and Ad5 sequence starting" from 9.24 map units of an adenovirus genome. It is not clear whether the adenovirus sequences present comprise sequences from 9.24 to 100 map units or not. The specification also states that a unique Swa1 restriction site replaces the Nde1 site located in the fiber gene. Although the level of skill for one skilled in the art is high for making recombinant plasmids, the skilled artisan is required to have some guidance for where the components of each plasmid are located in order to generate an identical clone of the vector claimed. It is not evident from the teachings in the disclosure whether the Pac1-Not1 site SV40pA signal Sal1-SacII components are within the Ad5 sequence starting" from 9.24 map units or not or if they are in the consecutive order listed in the claim and are outside the adenovirus sequence. In reference to the Swa1 sequence, it is not clear whether there is only one Nde1 site located in the fiber gene. There is no other guidance provided in the specification for how to make these plasmids and there is also no disclosure provided indicating where the structural elements of the plasmids are located. For these reasons, it is determined that the skilled artisan would be unable to make the instant plasmids. The skilled artisan is also unable to use plasmids that are not readily available and cannot be readily identified.

In conclusion, due to the lack of guidance provided in the specification for how to make the instant plasmids claimed, the lack of description for component order within the plasmids,

the lack of working examples demonstrating how to make the instant plasmids, the lack of prior art for these plasmids that would indicate that how to make these plasmids are well known, it is determined that an undue quantity of experimentation would be required of the skilled artisan to make or use the plasmids claimed or the method of using these plasmids to generate recombinant adenoviruses.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 36 and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Aoki et al. (Molecular Medicine. 1999; 5: 224-231) and He et al. (US 5,922,576).

The claims are drawn to a method of producing a recombinant adenovirus consisting of transfecting a host cell with an adenovirus backbone plasmid comprising an adenovirus genome lacking map units 0 to 9.2 and a shuttle plasmid comprising adenovirus sequences from 0 to 1 map units and 9.2 to 16.1 map units of an adenovirus genome. The transfection method is by calcium phosphate.

Aoki et al. teach an adenovirus backbone plasmid lacking map units 0-9.2 starting with the lefthand ITR and a shuttle plasmid comprising Ad map units 0-1 and 9.2 to 16.1, see the "Results" section on starting on page 226 and Figure 1 on page 227. Aoki et al. do not teach a transfecting a host cell by calcium phosphate.

However, He et al. teach generating a recombinant adenovirus by homologous recombination by co-transfecting adenovirus shuttle and backbone plasmids by calcium phosphate reagents. See Figure 1 and column 4, lines 20-31.

One of ordinary skill in the art at the time the invention was made would have been motivated to co-transfect the adenovirus plasmids of Aoki et al. with the transfection method of He et al. to generate recombinant adenovirus in a one-step process for *in vivo* assembly. One of ordinary skill in the art at the tine the invention was made would have had a reasonable expectation for producing the claimed invention because both references use shuttle and backbone plasmids to produce recombinant adenovirus. One of ordinary skill in the art at the time the invention was made would have had further expectation of success for using the plasmids of Aoki et al. in the transfection method of He et al. because all of the plasmids used in each of the references comprise overlapping adenovirus sequences that recombine by homologous recombination. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results to the contrary.

On page 6 of the response filed 12/25/02, applicant argues that the Aoki et al. does not anticipate the instant plasmids.

Applicant's arguments, as well as a careful consideration of the claims, have been considered, but are found unpersuasive because the instant plasmids "comprise" certain elements. This open transitional claim language does not exclude any additional element from the plasmids. Therefore, the addition of additional ingredients within the plasmids of Aoki et al. still fall within the scope of the claims.

Applicant also argues that Aoki et al. teach away from using homologous recombination since the reference teaches awareness of homologous recombination and chooses to improve upon it.

Applicant's arguments have been carefully considered, but are found unpersuasive. Although it is conceded that Aoki et al. improves homologous recombination, the plasmids Aoki et al. use comprise overlapping sequences, which are all that is required for homologous recombination to work in generating recombinant adenoviral vectors, see column 2, lines 25-42 of He et al. Therefore, should the loxP sequence within the plasmids of Aoki et al. be removed, the sequences would still recombine in the method of He et al. Further, the teachings of He et al. clearly indicate the generating adenoviruses by homologous recombination is widely used in the art. Therefore, it would be obvious for one of ordinary skill in the art to use the conventional method of He et al. or the method of Aoki et al. to generate recombinant adenoviruses with the plasmids of Aoki et al.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shanon Foley whose telephone number is (703) 308-3983. The examiner can normally be reached on M-F 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (703) 308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4426 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Shanon Foley
March 3, 2003

JAMES HOUSEL 3/10/03
SUPERVISORY PATENT EXAMINER
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